

Patient and kidney graft survival rates after first and second kidney transplantation

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Abstract

Introduction. Expanding donation criteria is one way of solving the problem of the increasing need of transplantation. The article is dedicated to comparison of the outcomes of first and second repeated kidney transplantation using grafts from standard criteria and expanded criteria donors.

Aim. To evaluate 1-year and 5-year recipient and kidney graft survival rates after first and second kidney transplantation according to the donor type – standard criteria or expanded criteria donors.

Material and methods. From 2007 till 2019 we performed 1459 kidney transplantations. The comparison study of outcomes of first (n=196) and second (n=143) kidney transplantations from standard criteria (n=245) and expanded criteria (n=94) donors was made.

Results. There were no significant differences in a 1-year patient survival according to the donor type (98% and 95%, $p=0.13$). A 5-year recipient survival was significantly poorer after kidney transplantation from expanded criteria donors (97.6% and 88%, $p=0.01$). There were no significant differences in 1-year and 5-year graft survival rates according to the order of transplantation ($p=0.21$ and $p=0.36$). We found no significant difference in 1-year recipient survival after kidney transplantation from expanded criteria donors according to the order of transplantation ($p=0.50$). A 5-year recipient survival was significantly difference poorer after second kidney transplantation from expanded criteria donors ($p=0.04$). One-year and 5-year graft survival rates were significantly lower after kidney transplantation from expanded criteria donors (94%, 88% vs. 86%, 65%, $p=0.0025$ and $p=0.0011$, respectively). One-year and 5-year survival rates were higher after first kidney transplantation from standard criteria donors in comparison with second kidney transplantation ($p=0.052$ and $p=0.02$, statistically significant in

both cases). Analyzing outcomes of kidney transplantation from expanded criteria donors we found 1-year and 5-year graft survivals to be higher after first kidney transplantation comparing with second kidney transplantation ($p=0.030$ and $p=0.018$, statistically significant in both cases).

Conclusion. *In case of second organ transplantation, it is reasonable to use organs from standard criteria donors.*

Keywords: first kidney transplantation, repeated (second) kidney transplantation, outcomes, recipient survival, kidney graft survival

CI, confidence interval

KT, kidney transplantation

RAG, renal allograft

Introduction

Kidney transplantation provides a significant advantage in patient survival and a better quality of life for a recipient compared to these parameters in patients receiving dialysis therapy. Due to the progressively increasing need for kidney transplantation in many patients, waiting for surgery takes an increasingly long period of time. One of the ways to solve this problem is to expand the criteria for the suitability of kidney grafts [1, 2]. The data from comparative studies of kidney transplantation from standard and expanded criteria donors published in the available medical literature are mixed. So, in 2008, J. Pascual et al. performed a meta-analysis of MEDLINE and EMBASE data on kidney transplant outcomes from standard criteria donors and expanded criteria donors. According to most reports, kidney transplants from expanded criteria donors were characterized by a poorer long-term survival. Only a few single-center observational studies have shown that the patient and graft

survival rates achieved when using kidneys from expanded criteria donors were similar to the patient and graft survival rates achieved when using kidneys from standard criteria donors [3].

In 2014, M. Koukoulaki (Greece) published an analysis of the outcomes of 310 kidney transplants, according to which the 1-, 3- and 5-year survival rates of kidney grafts from expanded criteria donors were 92%, 82% and 70%, and the recipient survival rates were 95%, 87% and 82%, respectively. When comparing these parameters with those of the patients who received organs from standard criteria donors, the 3-year survival of kidney grafts from expanded criteria donors was statistically significantly lower ($p < 0.0001$) [4].

Two independent studies conducted in the Republic of Korea in 2014 and 2018 reported that there were no statistical differences in the survival of recipients and kidney grafts obtained from donors with standard or expanded criteria. J.K. Hwang et al studied the results of 196 kidney transplantations. The 1- and 5-year survival rates in renal allograft (RAG) recipients from expanded criteria donors were 96.8% and 89.3%; 98.1% and 95.4% in RAG recipients from standard criteria donors, respectively. The 1- and 5-year survival rates of kidney grafts from expanded criteria donors were 93.5% and 76.3%; and of those from standard criteria donors were 93.8% and 89.2%. There were no statistical differences in recipient ($p = 0.563$) and graft survival ($p = 0.111$) rates between the two study groups [5]. K.J. Ko et al. analyzed the results of 405 kidney transplants from post-mortem donors. The 1- and 5-year graft survival rates were 94.4 and 86.3% in the group of recipients who received RAG from standard criteria donors, and were 94.1% and 80.9% in the group of recipients who received RAG from expanded criteria donors; 1- and 5-year survival rates of patients in the pertinent groups were 98.3%, 94.7% and 96.7%, 94.4%, respectively. There were no

statistically significant differences in the graft survival ($p=0.394$) and patient survival ($p=0.737$) rates [6].

In 2016, a meta-analysis which included 32 publications was conducted in France to assess the differences between kidney transplants from standard criteria donors and expanded criteria donors. The study considered also the geographical location of the transplant center. It was found that the relative differences between the groups of recipients who received organs from standard donors and expanded criteria donors were less pronounced in Europe than in North America [7].

F.J. van Ittersum et al. (Netherlands, 2017) noted in their study that kidney grafts from expanded criteria donors had a less favorable prognosis than grafts from standard donors, especially if they were transplanted to young recipients (younger 60 years old) or recipients with diabetes [8].

E. Ferreira et al. (Portugal, 2017) published data from a retrospective analysis of 617 kidney transplants. They noted that the patient and graft survivals were lower in the group of recipients who received the kidney graft from expanded criteria donors, but the statistically significant difference was found only in a 3-year graft survival censored by death and in a 5-year graft survival uncensored by death [9].

The report by A.H. Querard et al. (France, 2018), which analyzed the outcomes of 4833 kidney transplants, showed a 1.75-fold (95% confidence interval [CI] 1.53–2.00, $p < 0.0001$, statistically significant) increase in the risk of graft function loss in the patients who received a kidney graft from an expanded criteria donor, compared to organ transplants from standard donors. The 3-, 6-, and 10-year graft survival rates after kidney transplantation from expanded and standard criteria donors were 77%, 62%, 40%, and 82%, 68%, 53%, respectively [10].

Thus, in our opinion, a comparative assessment of recipient and graft survival rates in transplants from standard donors and expanded criteria donors in Russia is rather relevant.

The aim of the study was to evaluate the 1- and 5-year survival rates of recipients and kidney grafts depending on the donor type: either standard or expanded criteria donors as for the first and second transplantation.

The objectives:

1) To determine the kidney recipient survival rates depending on the donor type.

2) To determine the recipient survival rates after the first and second kidney transplants from standard donors.

3) To determine the recipient survival rates after the first and second kidney transplants from expanded criteria donors.

4) To determine the kidney graft survival rates in groups depending on the type of donor.

5) To determine the kidney graft survival rates when transplanted from standard donors after the first and second transplantations.

6) To determine the kidney graft survival rates when transplanted from expanded criteria donors after the first and second transplantations.

7) Evaluate the obtained data.

Material and methods

The study was based on a retrospective analysis of the results of 339 kidney transplantations performed at N.V. Sklifosovsky Research Institute for Emergency Medicine in the period from 2007 to 2019, and on assessing the condition of recipients treated at the Moscow City Scientific and Practical Center of Nephrology and Transplanted Kidney Pathology of Moscow city Clinical Hospital № 52. The criteria for

inclusion in the study were the first and second (repeated) kidney transplantation from a cadaveric donor. The exclusion criteria were the combined transplantation of kidney and other organs, a related donor KT, and KT with missed data on the donor type. Of 1316 recipients with the first KT, the sample (n=196) was stratified by recipient gender, age, and the donor organ type; there were 143 recipients with repeated KT. The distribution criterion for groups was the donor type (a standard or expanded criteria donor), the one for subgroups was the ordinal number of transplantation (either the first or the second one). Thus, the first group consisted of RAG recipients from standard criteria donors (n=245), the second group included those with RAG from expanded criteria donors (n=94). Subgroup A (n=134) comprised the recipients undergoing first KT from standard criteria donors; subgroup B (n=111) included the recipients after the second KT from the standard criteria donors, subgroup C (n=62) included the recipients after the first KT from expanded criteria donors, and subgroup D (n=32) were the recipients after the second KT from expanded criteria donors.

Recipients of Groups I and II were comparable in most parameters. Differences were found in age and body weight (Table 1). Thus, the kidney recipients from expanded criteria donors were statistically significantly older and more overweight. There were no differences between the groups in gender, sensitization, and the ratio of first and second transplants.

Table 1. Main characteristics of recipients with regard to donor type

Recipients, n	All 339	I 245	II 94	p
Age, m (25-75%), years	45 (35–55)	42 (32; 50)	55 (48; 60)	<0.05
Age range	18–72	18–72	31–72	
Males,% (n)	57.2 (194)	56.7 (139)	58.5 (55)	0.77
Females,% (n)	42.8 (145)	43.3 (106)	41.5 (39)	
Body mass index, kg/m ² , m (25-75%)	24.5 (21.5; 28)	23.7 (21; 27.1)	26.4 (23.4; 30.6)	<0.05
Intact, % (n)	44.5 (151)	41.6 (102)	52.1 (49)	0.13
Sensitized, % (n)	37.8 (128)	39.6 (97)	33 (31)	
No data, % (n)	17.7 (60)	18.8 (46)	14.9 (14)	
First KT,% (n)	72.3 (245)	54.7 (134)	66 (62)	0.06
Second KT,% (n)	27.7 (94)	45.3 (111)	34 (32)	

Among the diseases that had lead to chronic renal failure, the chronic glomerulonephritis and chronic pyelonephritis were the most commonly detected. The structure of the diseases is shown in Fig. 1.

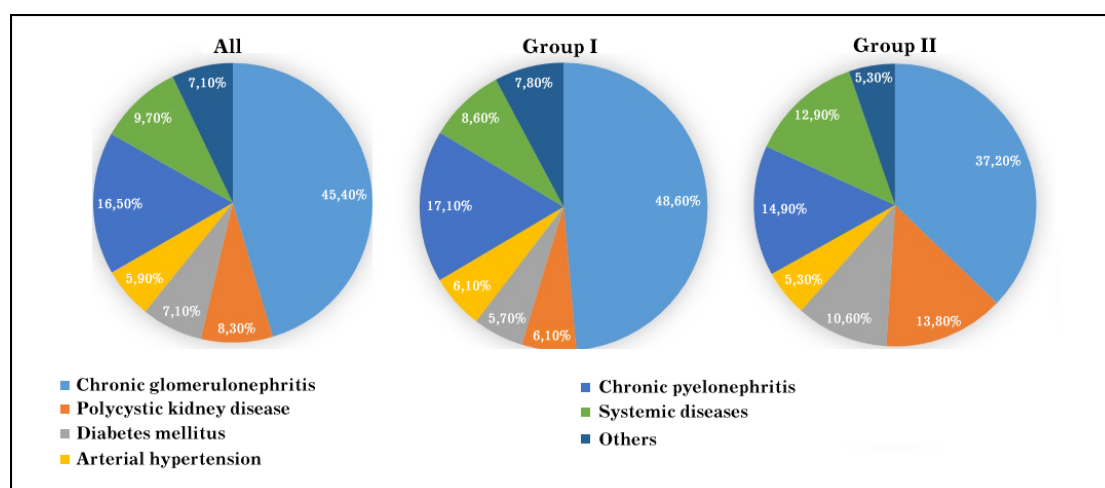


Fig. 1. The structure of the underlying diseases leading to chronic renal failure

There were no statistically significant differences between the groups in donor's gender, the graft cold ischemia time, and the number of HLA mismatches (Table 1). 2).

Table 2. Characteristics of donor and operational factors of both groups

Number of donor organs / transplants, n	All 339	Group I 245	Group II 94	P
Donor gender:				
Male,% (n)	68.4 (232)	68.6 (168)	68.1 (64)	0.81
Female,% (n)	30.7 (104)	30.2 (74)	31.9 (30)	
No data,% (n)	0.9 (3)	1.2 (3)	0	
Donor's age, m (25–75%), years	47 (38; 54) 18–69	42 (33; 48) 18–58	56 (54; 60) 40–69	<0.05
Cold ischemia time, m (25–75%), hours	13.5 (11; 16)	13 (11; 16)	14 (12; 16.5)	0.14
The number of HLA mismatches, m (25-75%)	4 (3; 4)	4 (3; 4)	4 (3; 4)	0.97

The age of donors in group II was significantly higher, which makes sense, as, according to the definition of the United Network of Organ Exchange (UNOS), the expanded criteria donor is a donor older 60 years or over the age of 50 with at least two of the following three conditions: the history of arterial hypertension, the terminal level of serum creatinine 1.5 mg/dL or above, or death as a result of cerebrovascular accident [3].

Immunosuppressive therapy: all patients received a three-component baseline immunosuppressive therapy consisting of calcineurin inhibitors, inosine monophosphate dehydrogenase inhibitors or proliferative signal inhibitors, as well as corticosteroids. Induction immunosuppressive therapy in most cases consisted of chimeric monoclonal CD-25 antagonist antibodies or lymphocyte-depleting antibodies (group I, n=207 [84.4%]; group II, n=80 [85.1%]).

Statistical analysis of the obtained data was performed using the Statistica for Windows, v. 12.0, software package, StatSoft Inc. (USA). The normality of the distribution was evaluated by the Shapiro-Wilk test. To compare groups, we used the Mann-Whitney test, the Fisher's exact test (two-sided), and the χ^2 test for four-field and arbitrary tables. P was considered statistically significant at $p < 0.05$. The Kaplan–Meier method was used for survival analysis. Survival rates in the groups were compared using a log-rank test. Confidence intervals of survival were considered by the Weibull analysis. Survival curves were calculated starting from the date of surgical treatment.

Results and discussion

The 1-and 5-year survival rates of group I recipients were 98% (95% CI: 97-99), and 97.6% (95% CI: 96-99), those of Group II were 95% (95% CI: 91-98), and 88% (95% CI: 82-93), respectively (Fig. 2).

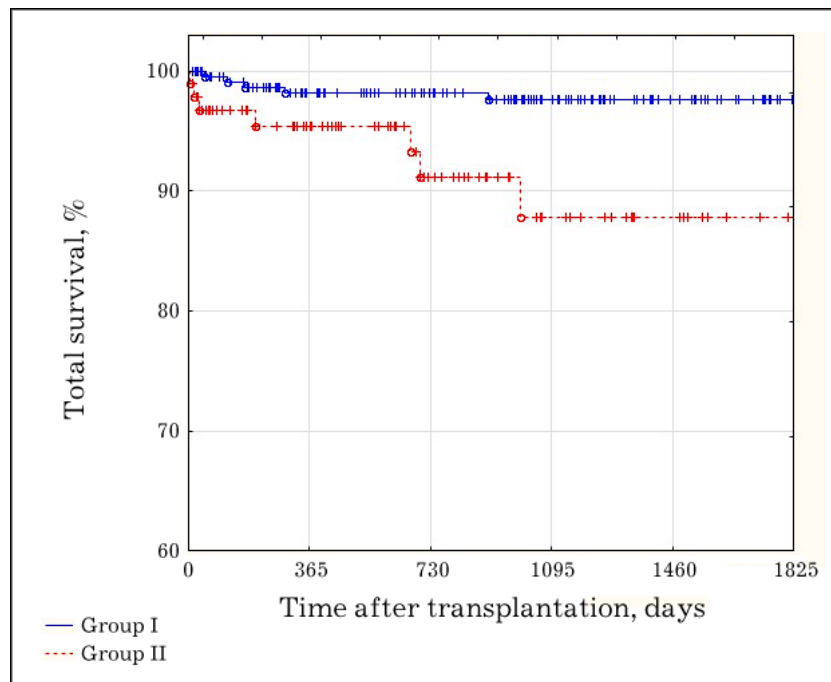


Fig. 2. Kidney recipient survivals with regard to the donor type (Kaplan-Meier)

When comparing a 1-year recipient survival rate, no differences were found between the groups, ($p=0.13$), but when comparing the 5-year survival rate, there was a statistically significantly lower survival rate of recipients in group II ($p=0.01$).

The 1- and 5-year survival rates of recipients who underwent the first kidney transplantation from standard donors (subgroup A) was 99% (95% CI: 98–100) each (for both periods); and they were 97% (95% CI: 94–99), and 96% (95% CI: 92–98) after the second kidney transplantation (subgroup B) (Fig. 3).

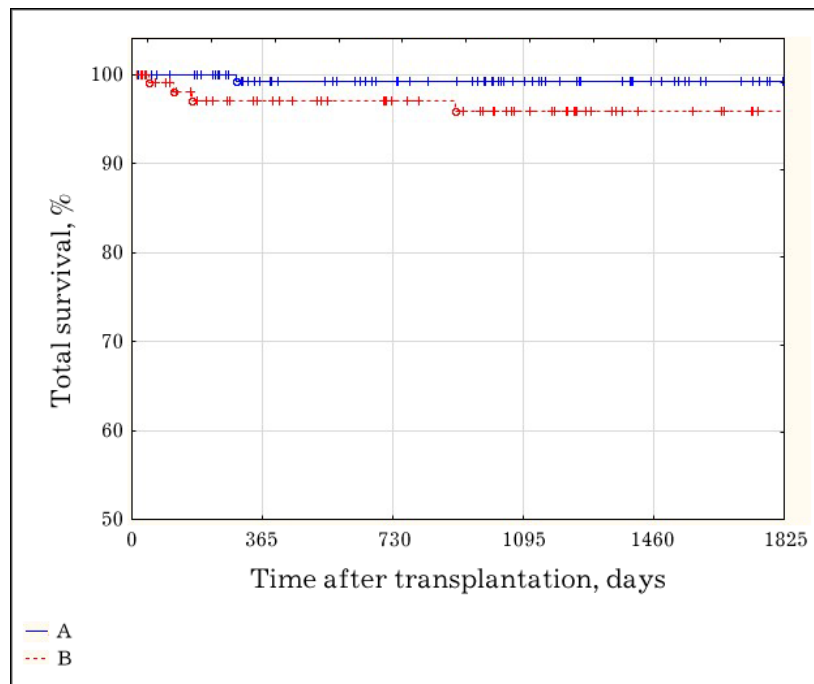


Fig. 3. Recipient survivals after first (A) and second (B) kidney transplantations from standard criteria donors (Kaplan-Meier)

There were no statistically significant differences in the 1- and 5-year survival rates of kidney recipients from standard donors depending on whether the transplant was performed as the first or the second ($p=0.21$, and $p=0.36$). Thus, it was determined that the fact of either it

was the first or the second/repeated transplantation did not affect the 1- and 5-year survival rates of kidney recipients from standard donors.

The 1- and 5-year survival rates of the recipients were 96% (95% CI: 92–99) each (for both periods) after the first kidney transplantation from expanded criteria donors (sub-group C), and 94% (95% CI: 86–99), and 74% (95% CI 63–87) after the second one (subgroup D) (Fig. 4).

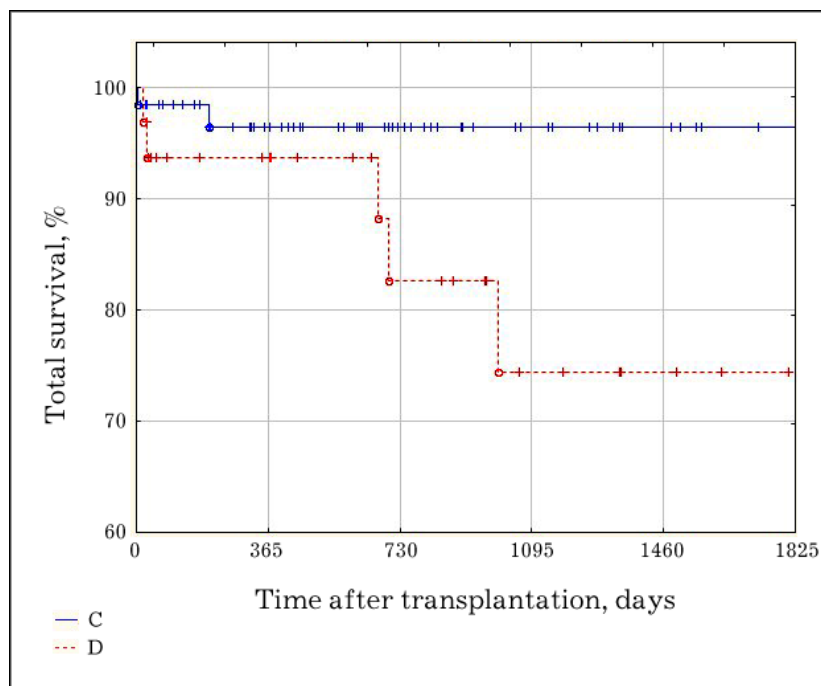


Fig. 4. Recipient survivals after the first (C) and second (D) kidney transplantations from expanded criteria donors (Kaplan-Meier)

There were no statistically significant differences in the 1-year survival of kidney transplant recipients from expanded criteria donors, depending on whether the first or second transplantation was performed ($p=0.50$). However, when comparing the 5-year survival rates of recipients from expanded criteria donors, they were found statistically significantly lower after the second kidney transplant than after the first one ($p=0.04$).

Thus, the 1- and 5-year kidney graft survival rates were 94% (95% CI-92-97) and 88% (95% CI-84-91) in group I, and 86% (95% CI: 80-91) and 65% (95% CI: 58-74) in Group II, respectively (Fig. 5).

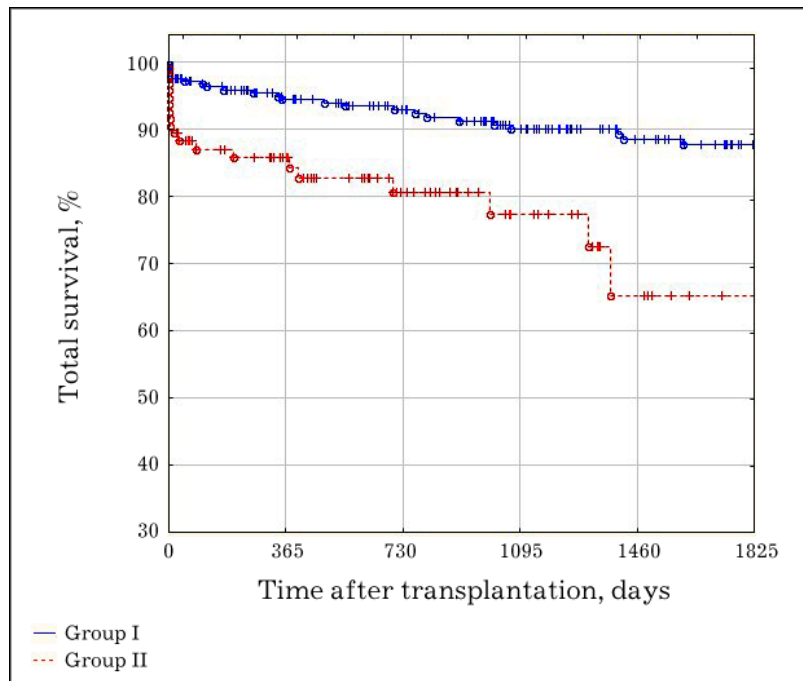


Fig. 5. Renal graft survivals in the study groups (Kaplan-Meier)

When comparing the 1- and 5-year RAG survival rates between the recipients of groups I and II, a statistically significant difference was found ($p=0.0025$ and $p=0.0011$). Thus, in the group of kidney recipients from expanded criteria donors, the graft survival rate was statistically significantly worse than in the group of recipients from standard donors, which corresponds to most studies from Europe and America.

So, 1- and 5-year kidney graft survivals were 97% (95% CI: 94–99) and 93% (95% CI: 89–96) in subgroup A, 90% (95% CI: 87–95) and 81% (95% CI: 75–87) in subgroup B, respectively (Fig. 6).

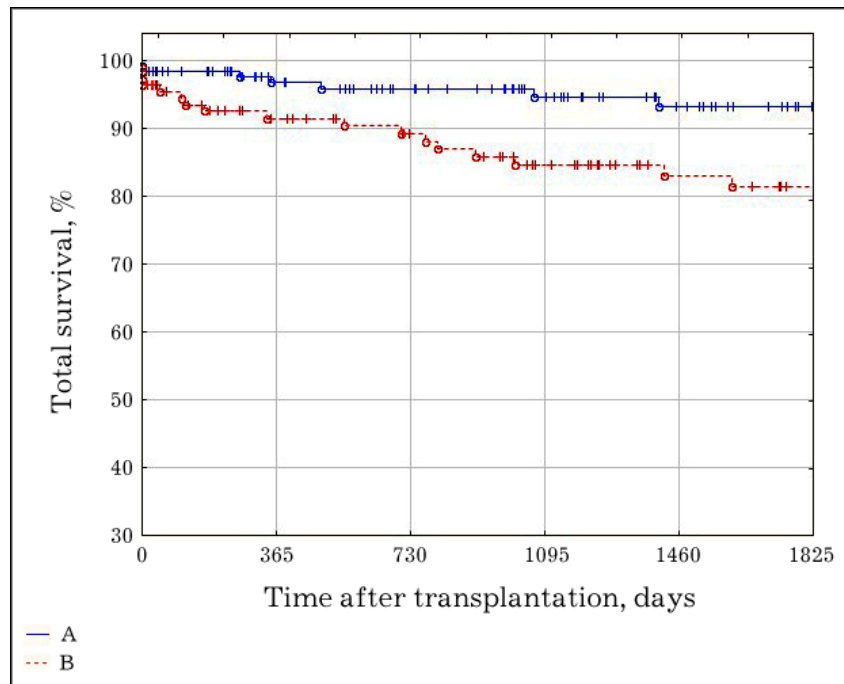


Fig. 6. Survival of renal grafts from standard criteria donors after the first (A) and second (B) transplantations (Kaplan-Meier)

When comparing the 1- and 5-year survival rates of kidney grafts from standard donors, higher rates were found after the first transplant than after the second ($p=0.052$ and $p=0.02$). The data obtained indicate a statistically significantly better 5-year survival rate of kidney grafts from standard donors as a result of the first transplantation than the second one.

One- and 5-year survivals of kidney grafts were 91% (95% CI: 85–96) and 78% (95% CI: 70–86) in subgroup C, and 75% (95% CI: 63–87) and 46% (95% CI: 36–64) in subgroup D, respectively (Fig. 7).

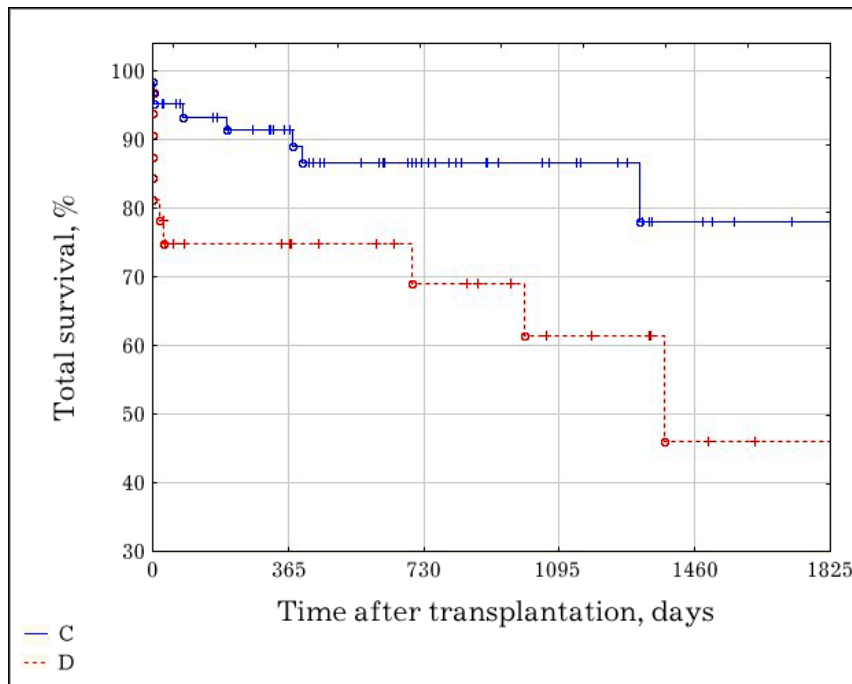


Fig. 7. Survival of kidney grafts from expanded criteria donors after the first (C) and second (D) transplantations (Kaplan-Meier)

When comparing the 1- and 5-year survival rates of kidney grafts from expanded criteria donors, higher rates were found after the first transplantation than after the second ($p=0.030$ and $p=0.018$, statistically significant in both cases), which indicates the worse results of repeated kidney transplantation from expanded criteria donors. It should be noted that most of the unsatisfactory results of kidney transplantation from expanded criteria donors during the first year after transplantation were associated with the lacking RAG function recovery, i.e., the development of a primary non-functioning graft.

However, the interest in using organs from expanded criteria donors for kidney transplantation is understandable. More kidney transplants will lead to shorter waiting times and lower morbidity and mortality associated with a long-term dialysis therapy. Some investigators recognize that kidney transplantation from expanded criteria donors provides quite satisfactory survival rates for patients and grafts, despite

their less satisfactory long-term results [4, 9]. A number of transplant specialists, based on the available data, come to the conclusion that patients younger than 40 years, recipients for kidney re-transplantation or with diabetes should not receive kidneys from expanded criteria donors [3, 8]. The 5-year survival rates of kidney grafts from expanded criteria donors were 70% and 80.9% in Greece and Korea; in our clinic, they were 75% for the first kidney transplantation and 46% for the second transplantation. Comparing these figures, we can speak about unsatisfactory long-term survival of kidney grafts from expanded criteria donors for repeated transplantation.

Evaluation of the graft and recipient survival rates in our study showed that kidney transplantation from expanded criteria donors has shown satisfactory graft and recipient survival rates, except in the cases of repeated transplantation. Therefore, for this category of recipients, we consider kidney transplantation from standard donors to be justified.

Conclusions

1. There were no statistically significant differences in a 1-year recipient survival rates between the kidney recipients from standard criteria donors and expanded criteria donors: 98% and 95%, respectively ($p = 0.13$).

2. A 5-year survival of kidney recipients from standard criteria donors was statistically significantly better than from that of expanded criteria donors 97.6 versus 88% ($p = 0.01$).

3. The 1- and 5-year recipient survival rates in kidney transplant recipients from standard criteria donors did not significantly differ statistically between those after the first and second kidney

transplantations 99%, 99%, and 97%, 96%, respectively ($p = 0.21$; $p = 0.36$).

4. There were no statistically significant differences in the 1-year recipient survival rates after the first and second kidney transplants from expanded criteria donors: 96% and 94%, respectively ($p = 0.50$).

5. A 5-year survival of kidney recipients from expanded criteria donors is statistically significantly better after the first transplantation than after the second one, 96% and 74%, respectively ($p = 0.04$).

6. The results of 1- and 5-year survivals of kidney grafts from standard criteria donors were statistically significantly better than those from expanded criteria donors: 94%, 88%, and 86%, 65%, respectively ($p = 0.0025$; $p = 0.0011$).

7. There were no statistically significant differences in a 1-year survival of kidney grafts from standard criteria donors after the first and second transplantation: 97% and 90% ($p = 0.052$).

8. There were statistically significant differences revealed in a 5-year survival of kidney grafts from standard criteria donors after the first and second transplants: 93% versus 81% ($p = 0.02$)

9. One- and 5-year survivals of kidney grafts from expanded criteria donors are statistically significantly better with the first transplantation than with the second one: 91%, 78% and 75%, 46%, respectively ($p = 0.030$, $p = 0.018$).

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